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RADIUM

EDITED BY
CHARLES H. VIOL, Ph. D.
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WILLIAM H. CAMERON, M. D.

VOL. IX JUNE, 1917 No. 3

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A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES

RADIUM

A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY, PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES.

Edited and Published by Charles H. Viol, Ph. D., and William H. Cameron, M. D with the assistance of collaborators working in the fields of Radiochemistry, Radioactivity and Radiumtherapy.

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VOL. IX JUNE, 1917 No. 3

THE USE OF RADIUM IN CANCER OF THE PROSTATE AND BLADDER.

A PRESENTATION OF NEW INSTRUMENTS AND NEW METHODS OF USE.*

HUGH HAMPTON YOUNG, M. D., BALTIMORE

In 1913, Pasteau and Degrais reported a few cases of cancer of the prostate and bladder in which truly striking results had been obtained by the use of radium introduced into the urethra through an ordinary catheter (Fig. 1). This led me, in 1914, to procure some radium and to try it in certain selected cases. It soon became evident that for accurate work much more exact methods and special instruments would be necessary, and in the machine shop of the Brady Institute I set about to design and construct instruments to meet the varying needs in vesical and prostatic cancer.

Fig. 1.—Catheter method of Pasteau and Degrais for applying radium in cancer of bladder and prostate.

The accompanying illustrations show the different models so well that little description is necessary. The small, straight cystoscope which is used in my cystoscopic rongeur (Fig. 2) was used as a basis around which to construct the various radium instruments.

*Reprinted from the Journ. American Med. Assn., Vol. LXVIII., pp. 1174-1177, April 21, 1917. From the James Buchanan Brady Urological Institute, Johns Hopkins Hospital.

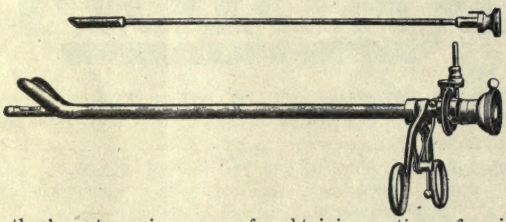

Fig. 2.—Author's cystoscopic rongeur for obtaining sections of vesical tumors for microscopic study.

Radium Instrument 1 (Figs. 3 and 4) carries the radium in its beak. The slender glass tube containing the radium is enclosed in a platinum capsule which slips easily into the open tubular end of the beak of the instrument and is held there by friction. The instrument

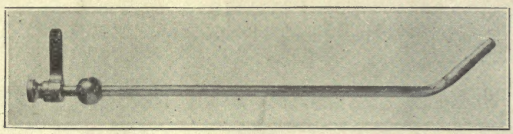

Fig. 3.—Author's Cystoscopic Radium Instrument 1 carrying a tube of radium in fenestrated platinum capsule in beak; closed with obturator.

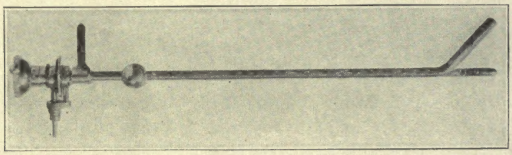

Fig. 4.—Instrument 1 with straight cystoscope introduced.

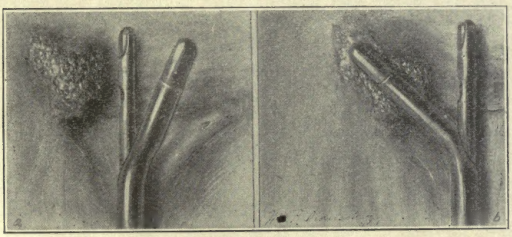

Fig. 5.—(a) Observation of tumor through cystoscope. (b) Application of radium capsule against tumor.

is passed through the urethra with an obturator (Fig. 3) which is then withdrawn, the bladder washed out and the cystoscope introduced (Fig. 4), making it possible to locate the region to be treated (Fig. 5 *a*) and to apply the capsule containing radium directly on it (Fig 5 *b*) When

in the proper position the instrument is held fixed by the mechanical hand attached to the cystoscopic table shown in operation in Figure 6. This instrument and accurate methods of use were demonstrated to several medical societies in 1915.

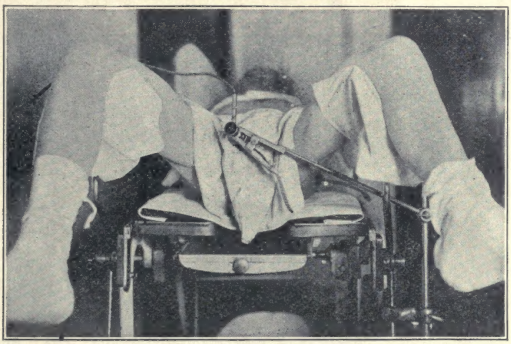

Fig. 6.—"Mechanical hand" or clamp holding radium instrument in position desired.

Radium Instrument 1 has proved satisfactory for application to the neck of the bladder, trigon and certain portions of the lateral and posterior walls. It is usually easy to see satisfactorily with the cystoscope and to place the radium directly on the lesion to be treated.

For tumors well out on the lateral walls of the bladder or on the upper part of the anterior wall this instrument is not satisfactory, as the end and not the length of the radium tube is presented to the tumor. On this account another instrument was necessary, and to meet this need I have devised a second instrument.

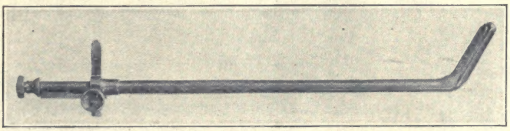

Fig. 7.—Author's Cystoscopic Radium Instrument 2 closed (radium in beak) with obturator.

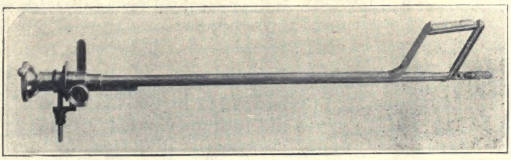

Fig. 8.—Instrument 2 opened ready for use in bladder

As shown in Figure 7, Radium Instrument 2 carries the capsule of radium within the beak, which is made up of two hollow halves which,

when separated by an external operating mechanism, carry the radium out to a position parallel to the shaft and about 2.5 cm. distant from it, as shown in Figure 8, in which it is in position to be placed against tumors quite remote from the middle of the bladder, as shown in Figure 9. This instrument has proved satisfactory in many such cases.

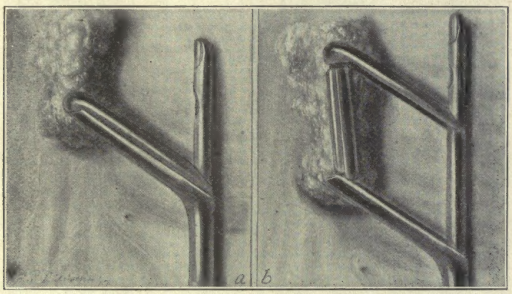

Fig. 9.—Instrument 2 in use: (a) inspection of tumor; (b) application of radium.

For tumors on the posterior wall of the bladder, still another instrument was desirable in order to place the radium broadside against them, as both instruments (1 and 2) here presented only the end of the radium tube to the posterior wall, and a third instrument was therefore designed, as shown in Figure 10.

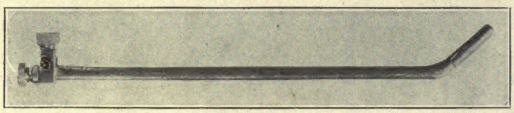

Fig. 10.—Author's Cystoscopic Radium Instrument 3 closed, with obturator.

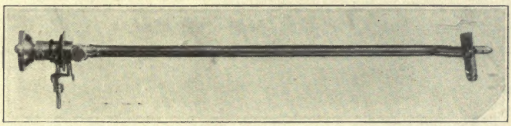

Fig. 11.—Instrument 3; beak with radium revolved for application to posterior wall.

As seen here, the beak carrying the radium revolves about its center (Fig. 11), being operated by two wires in the shaft and a screw outside. Figures 12 and 13 show the radium carried crosswise the shaft in position to be applied, under cystoscopic direction, to tumors on the posterior wall.

With these three instruments it is possible to place the radium flat (lengthwise) against a tumor in any part of the bladder, and to inspect it through the cystoscope from time to time, during the application. A

capsule with a fenestra along one side is usually employed in vesical tumors so that the radium may be placed unscreened directly against the neoplasm, but screened from the rest of the bladder. By this means we have been able to secure all the action of both beta and gamma rays, and at the same time have avoided burning the bladder in surrounding regions, thus making much longer treatments quite possible.

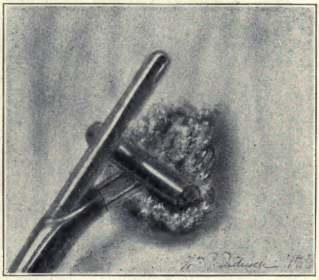

Fig. 12.—Instrument 3 in use against tumor on posterior wall of bladder.

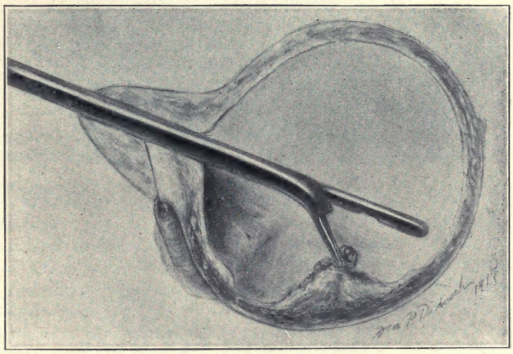

Fig. 13.—Sectional view, showing use of Instrument 3.

The duration and frequency of the treatments vary according to the case, the tolerance of the individual and the size of the tumor. The instrument is held in the desired position by the mechanical arm, described before, and the treatment continues an hour or more if possible. Intensive treatments are desirable, and in order to shorten the applications in sensitive cases several hundred milligrams of radium in a high percentage of purity are required to secure the best results. The treatments are made every two or three days, if possible, and a different site on the surface of the tumor attacked each time. We have seen many large tumors respond rapidly, but sometimes a few fulgurations may be helpful in causing large tumor masses to slough away quickly, so that the base can be reached for direct radium applications (Fig. 14).

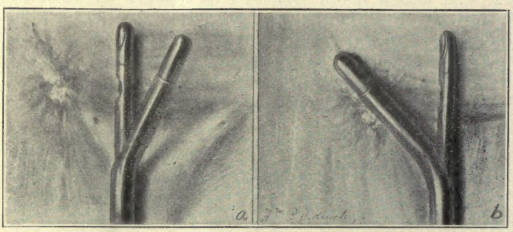

Fig. 14.—Application of radium to base of tumor destroyed by fulguration: (a) observation; (b) application.

Later, with Dr. William Frontz, I shall report at length on the results obtained, some of which have been quite remarkable.

In cancer of the prostate, Instrument 1 (Fig. 3) has proved satisfactory, not only for intravesical but also for intraurethral and rectal applications of radium. In the urethra and rectum the cystoscope is not necessary. I usually employ a nontubular instrument (Fig. 15): but a finger in the rectum tells definitely when the beak of the instrument carrying the radium capsule is in the desired place, and the mechanical arm holds it there (Fig. 16.)

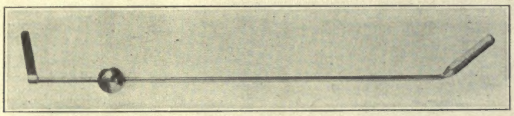

Fig. 15.—Rectal radium carrier, applied under direction of index finger in rectum, and held in place by mechanical hand or clamp.

In carrying out these treatments I make use of charts (Figs. 17, 18, 19). As shown here the size and extent of the cancers of the prostate, seminal vesicles and bladder are indicated in outline and the location of the treatments are given with the date and the number of milligram-hours affixed, thus showing everything graphically on one sheet. By this means the position of successive radium applications is varied from day to day so as to avoid overlapping and consequent burning, particularly when normal urethral or rectal mucosa intervenes between radium and tumor, as in cases of prostatic cancer.

By thus applying the radium at a different place each time it has been possible to accomplish as many as twenty-five transrectal treatments (each of one hour's duration) in cases of cancer of the prostate and seminal vesicles without producing any rectal burn or even marked irritation. Heretofore transrectal radium treatments of cancer of the prostate have been considered inapplicable on account of the vulnerability of the rectal mucosa. The methods here described make it possible to eliminate these complications, and greatly increase the ability for intensive treatment. With the instrument here described the radium (screened by a platinum capsule) can be applied, with the direction of a gloved finger in the rectum, accurately to almost any desired point of the carcinomatous prostate or seminal vesicles, and held there for an hour or more. Not infrequently a region above the seminal vesicle

along the lateral wall of the pelvis and adjacent to the sacro-iliac synchondrosis is reached in order to pass well above the upper limits of the disease and treat the lymphatics or glands of this region.

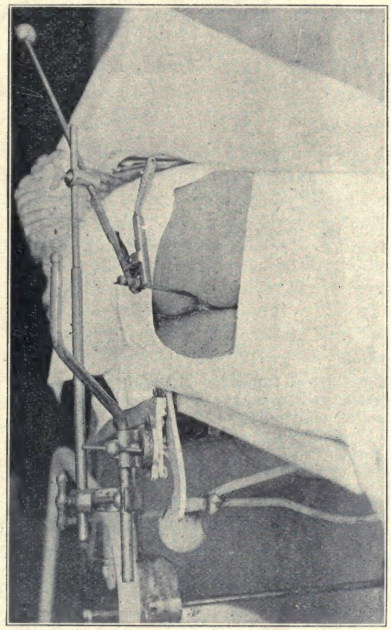

Fig. 16.—Mechanical hand in use in treating cancer of seminal vesicles and prostate through rectum.

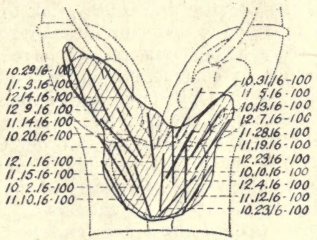

Fig. 17.—A case of cancer of the prostate and left seminal vesicle (right vesicle slightly involved). The radium treatments, each representing milligram hours, are shown, and the date of each is recorded.

The urethral and vesical mucosae have proved very tolerant to transurethral and transvesical treatments of cancer of the prostate and seminal vesicles. Not infrequently from 200 to 300 milligram-hours at one seance have been borne by the urethra or bladder without burn or evident irritation. The deep urethra affords three nonoverlapping positions for trans-urethral radiation, and each of these may be again used

without fear in two weeks or more. Four or five transvesical positions are available for treatment of the seminal vesicle, and at the prostatic orifice the beak of the instrument may be turned in various directions against as many different enlarged lobes as may be present.

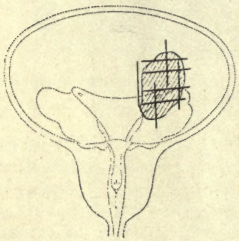

Fig. 18—Chart of a case of tumor of bladder (involving left ureter) showing radium treatment given with Instruments 1 and 2.

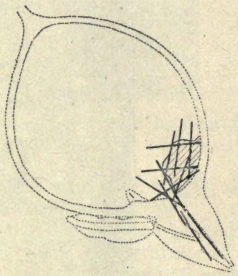

Fig. 19.—Chart of treatments given tumor of anterior wall of bladder near prostate.

I began this radium work timidly and cautiously, as I was fearful of injury caused by burns from short urethral or rectal treatments. The methods described above were evolved slowly, step by step, after we had demonstrated that by exact methods it was possible to place the radium where we willed and to change its location sufficiently often to avoid injury of normal intervening adjacent or remote structures. By these means far greater localized treatment, made directly on the neoplasm or through an insignificant layer of intervening mucous membrane, has become possible. I have also used radium in prostatic hypertrophy cases in which the patient was too desperately sick to be operated on.

This article is not intended to speak of ultimate results, but we may safely say here that truly astonishing results have been obtained in some cases: disappearance of obstruction, shrinkage and great softening of certain cancers of the prostate, and extensive retrogressive changes in inoperable cancers of the bladder. Fairly large amounts of radium, in high concentration, are desirable in order to make the treatments, amounting to 200 or more milligram-hours, of as short duration as possible. This is particularly true of cancers of the bladder, in which the patient is often intolerant of long treatments.

These methods have opened up a new and fertile field of therapeutics in a class of urologic cases which have heretofore been almost beyond relief. While we do not as yet know all the possibilities of cure, we do know that much relief can be afforded.

THE PALLIATIVE TREATMENT OF INOPERABLE CARCINOMA OF THE CERVIX BY MEANS OF RADIUM*

ROBERT T. FRANK, M. D.

From the First Gynecological Service of Mt. Sinai Hospital, New York, and Columbia University, George Crocker Special Research Fund, Dr. F. C. Wood, Director.

The various palliative treatments formerly employed in cases of inoperable carcinoma of the cervix have proved so unsatisfactory that any improvement should be hailed with joy by the profession. Reports of the success of radium treatment, therefore, deserve attention and investigation, since these reports have appeared in the last few years with such frequency that the method may now be considered firmly established. The technique and application, the range of usefulness, the permanency of the relief, the histological changes taking place, and the process by which the rays produce their effects are, however, questions which are still unsettled; and the purpose of this article is to contribute to the various phases of the subject not yet cleared up, and to put on record sundry interesting observations made during the treatment of a small but varied series of cases.

Under ordinary circumstances, it would be unwise to report such a series of cases at so early a stage of treatment; but as no claim is made that permanent results have been obtained, it has been thought permissible to describe the early palliative effects, without attempting to predict whether the improvement is more than temporary.

The writer has treated twelve cases of carcinoma of the cervix in the gynecological wards of Mt. Sinai Hospital, eleven on the service of Dr. Joseph Brettauer, and one on that of Dr. H. N. Vineberg. He takes this occasion to thank Dr. Brettauer and Dr. Vineberg for putting the cases at his disposal. Two patients withdrew from treatment and were lost sight of after two radiations each, before the result could be observed. His technical experience has been enlarged by the treatment of fourteen other patients, including those suffering from vulvar, rectal, gastric, laryngeal, etc., conditions; these, however, will not be referred to, as they do not bear directly upon the subject discussed in this paper.

Radium employed. Through the kindness of Dr. Francis Carter Wood, radium bromide, equaling 130 mgm. of pure radium, was placed at the disposal of the writer. The radium was distributed in four glass tubes containing respectively 83, 20, 17, and 10 mgm. The length of the largest tube (28.7 mm.) at times made awkward its application within the vagina. In most instances, 120 mgm. were used; in some cases, only 47 mgm. were employed.

TECHNICAL.

Screening. As it is essential that the soft alpha and beta rays be removed by filtration, brass or lead was interposed between the glass radium container and the tissues. These metal filters in turn generate soft secondary rays which are as destructive to the tissues as the soft primary rays, but the secondary rays are steadily absorbed by para rubber, gauze, or paper.

*Reprinted from The Journal of Cancer Research, II. pp. 85-102- Jan, 1917.

Preparation of radium carrier. The radium was arranged differently in each case, depending upon the site of the lesion, the size of the growth, and the dimensions of the vagina.

1. If 47 mgm. only were used, the three naked glass tubes of 10, 17, and 20 mgm. were placed in a hollow lead cup attached to a handle. The opening was covered with a lid of brass, 1 to 1.5 mm. thick, which was fastened with a layer of adhesive plaster, and the cup was inclosed in a small bag of rubber, 1 mm. thick (fig. 1). The use

A B C D E F

Fig. 1. Instrumentarium Used for Radium Application to Uterus Cervix and Vagina.

A, Hollow lead cup on handle, showing brass cover attached with adhesive plaster and thrown back. B and D, Brass container for 17 and 10 mgm. capsules of radium. C, Thinner walled lead cup without cover. E, Brass containers in tandem arrangement for radiation of corpus carcinoma. F, Numerous layers of lead foil which are used to protect healthy parts.

of the lead cup was suggested to the writer by Dr. Howard A. Kelly of Baltimore, who employs it in the treatment of cervical carcinoma. The cup has the advantage that the rays are cut out in every direction but one, and that the attending nurse is able to change the direction of the rays without disturbing the patient. It is most useful in carcinomata of small size where concentration of the rays is desired.

2. For large cauliflower growths, especially such as were accompanied by diffuse downward infiltration of the vaginal walls, the follow-

Fig. 2. Trident Arrangement Convenient for Radiation of Large Growths Infiltrating the Vaginal Wall.

ing arrangement was found to be most advantageous: The 83 mgm. tube was inclosed in a brass capsule, 1.5 mm. thick, which was screwed to a handle. Around the periphery of this tube the three other tubes were placed in a similar container, but without handles. They were secured to the central tube with strips of adhesive plaster, surrounded with a rubber bag, and introduced as one (fig. 2). If, for example, the anterior vaginal wall be infiltrated, but the rectovaginal septum be unaffected, one side of the carrier may be additionally screened by four to eight thicknesses of lead foil, applied inside the rubber filter. If the lead protector be placed facing the rectum, this viscus is protected from unnecessary radiation, while the affected anterior wall receives a larger quantity of radiation.

3. In crater-like carcinomata, extending up into the cervix and involving the parametria, the arrangement was slightly varied, the long central tube being advanced 1 to 2 cm. in front of the three smaller tubes. This permitted the introduction of the projecting tube within the cervix, the smaller tubes at the same time radiating the vaginal portion and fornices (fig. 3).

Introduction of the carrier. The radium is introduced under guidance of sight, after the vaginal walls are separated with spades or retractors. Unless the carrier is to be introduced within the cervical canal, a layer of gauze about 0.5 cm. in thickness is interposed between the growth and the carrier. The carrier, fastened to the handle, is pushed firmly against the gauze, and then the vagina is tightly packed

with gauze, so that its walls are separated as far as possible from the radium. The handle is secured to the vulva with strips of adhesive plaster, exactly as a permanent catheter is fixed in position. A dressing and T binder complete the operation. Patients who suffer pain are given a liberal injection of morphine to keep them quiet and comfortable.

Length of application. It is rarely possible to introduce the radium for more than eighteen to twenty-four hours at one session, because the patient must remain quiet during the treatment. An application of 120 mgm. for twenty-four hours gave the large dosage of 2880 mgmhrs. (milligram hours). A considerable part of the radiation, however, is absorbed by the 1.5 mm. of brass or 0.5 to 2 mm. of lead, the 1 to 3 mm. of rubber, and the gauze, all of which are interposed between the radium and the tissues.

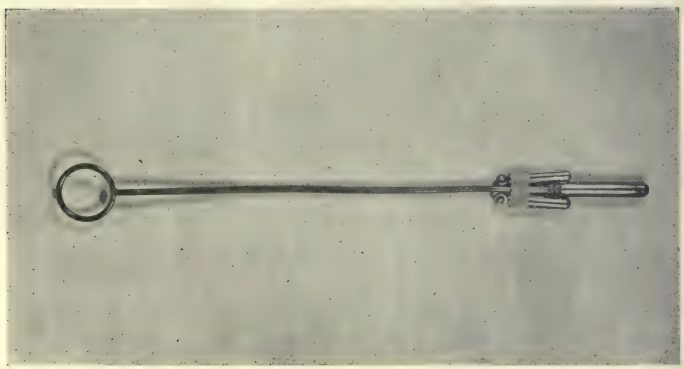

Fig. 3. Central Applicator Advanced to Permit Introduction Within Vaginal Canal, the Latter Containers Radiating the Portio.

Frequency of application. The frequency of application depends largely upon the local conditions, the amount of reaction (pain, rectal and bladder tenesmus, change in body weight, symptoms of absorption or toxemia), etc. In general, the following method has proved most satisfactory to the writer, but individual preference and experience will suggest wide variations. The further advanced the growth, the larger the initial dose indicated. The second treatment should be given seven to ten days after the first; the third treatment, fourteen days after the second. If improvement becomes apparent (cessation of pain, hemorrhage, and foul discharge, shrinkage and cleansing of the cancer surface), the next two treatments should be given at intervals of three weeks in diminishing dosage. For the first series 5000 to 6000 mgmhrs. are sufficient; and, thereafter, one treatment each month for two or more months completes the primary treatment. The patient should present herself for examination at least once in four weeks, in order that general appearance, general health, local conditions, and weight, may be observed. Should recurrence manifest itself, a new series of radiations may be undertaken.

CLINICAL.

Local effects of radiation. In every case so far treated a distinct amelioration of pain was observed within two weeks after the second radiation. Coincidentally, the bleeding diminished or disappeared, and the foul discharge became odorless and serous in character. In the earlier cases treated, because of insufficient filtration, very annoying rectal and vesical tenesmus was complained of, usually most marked on the third and tenth day after the beginning of the treatment. Severer rectal tenesmus developed in these cases as late as the third month. Since the practice of distending the vagina with gauze has been adopted, these unpleasant symptoms have either not appeared or have been very mild in character.

Between the third and fifth week after the beginning of the treatment, the cervix was observed to contract and shrink, assuming a characteristic senile size and conformation. The interior of the cervix and, sometimes, the vaginal portion were covered with a densely adherent, thick, yellow white, "bacon-like" exudate, which persisted for months. The thickening of the parametria and vaginal infiltration (much of which is usually of an inflammatory nature) gradually diminished. At a later date (after three to six months) the parametria again became more rigid (scar tissue?).

General effects of radiation. With the disappearance of the pain, bleeding, and discharge, the patient's general condition rapidly improved. In several instances (large, sloughy growths), a mild toxic condition, not marked by rise of temperature and transient in duration, was observed. In most cases, a rapid increase in weight was noted. Several of the patients appear to enjoy perfect health at present; in several others, a progressive loss of weight and strength and undefined pains and malaise are noted after a period of several months of well-being. In one of these, an enlarged nodular liver signifies hepatic metastases; in two others, in spite of the deterioration of health, no physical signs as yet denote recurrence.

Applicability of the treatment. (a) To advanced cases. Up to date, no case has been refused treatment. As will be noted from the histories, two cases had been given up as hopeless, after repeated local cauterizations (thermocautery) had proved even temporarily ineffective. One patient had had two operations (hysterectomy and secondary operation for recurrence) followed by local recurrence in the vaginal vault. In several instances, the recto- and vesicovaginal septa were involved. One patient with fracture of the humerus (x-ray diagnosis: "pathological fracture of the humerus, suspicious of metastatic involvement") is now under treatment.

The writer sees no contraindication to the treatment of even the most advanced cases. Even if no permanent relief is afforded, prompt cessation of pain, bleeding, and discharge can be obtained. A more merciful death from internal metastases or cachexia may then be anticipated. Only where carcinomatous perforation into the bladder or rectum is imminent, will radiation, by hastening the disintegration of the carcinomatous tissue, favor cloaca formation.

(b) To early cases. The operable cases of carcinoma of the cervix which have come under the writer's observation during the last ten years have been few in number (23). The final results of the radical operation, except in the hands of a few operators who control a large material, have been discouraging. In the light of the experience of

others and of the two cases reported below (cases 4 and 5), the writer feels inclined to advise, at least tentatively, that operable cases be subjected to a short preliminary treatment by radiation, followed by an abdominal total hysterectomy and salpingo-oophorectomy without excision of the parametria. It is, however, not justifiable, in the present state of our knowledge, to rely solely upon radium treatment in operable cases, unless the patient is an exceptionally poor risk (excessive obesity, severe cardiac, pulmonary, or renal disease), because there is as yet not sufficient evidence that a permanent cure can be produced by radium.

The preliminary radium treatment should be vigorous and short in duration. "Sterilization" of the growth should be sought, but the operation should be undertaken before the parametrial scar tissue formation, which regularly follows radiation, has had time to advance too far. In case 4, seven weeks elapsed between the beginning of treatment and the hysterectomy. The pelvic connective tissues were found to be so hard, contracted, and board-like, that the ureters could not be identified or pushed away from the uterine arteries. The operation consequently proved most difficult, and a transient ureterovaginal fistula subsequently developed.

Case 5 was, therefore, operated upon nine days after the beginning of radiation, and no such technical difficulties were encountered. On the other hand, microscopical examination of the carcinoma showed very few cytological changes, although the normal appearance of the cells did not necessarily exclude inhibition of cell division, the checking of division being the mode of action of radium on cells (fig. 11).

In view of these observations, the writer is inclined to advise preliminary radiation extending over a period of three weeks (three exposures of about 2000, 1200, and 800 mgm. hours each) followed within two to three days by hysterectomy. It appears inadvisable to operate before the lapse of three weeks, because the growth has not been sufficiently cleansed from a bacteriological point of view. Four weeks after operation, radium treatment should be resumed (at least three treatments at four weeks intervals).

HISTOLOGICAL

In every case a specimen was excised from the growth before the treatment was inaugurated. Usually a small specimen was removed before each subsequent radiation so that the cytological process could be followed from beginning to end. Toward the close of the treatments, however, difficulty is experienced in obtaining sufficient material, as the cervix becomes small, hard, and covered with a necrotic layer of detritus.

Figures 4, 5, 6, and 7 are photomicrographs of sections obtained from specimens taken at intervals during the course of treatment from Case 6. Figure 4 shows untreated squamous-cell carcinoma, figure 5, beginning nuclear alterations in the cancer cells; figure 6, far advanced cellular degeneration and vacuolation; figure 7, the final stage in which cell detritus, fibrin, and amorphous material predominate.

The first cellular changes are noted about ten days after the initial treatment. Rapid disintegration of the surface of the growth does not become apparent before three weeks have elapsed.

From observations made upon readily accessible carcinomata (massive carcinomata of the vulva, two cases), it has become evident that 1 to 1.5 cm. is about the maximum depth of cancer tissue at which the rays of 120 mgm. of radium exert their effect. Beyond this distance, the cancer cells appeared to be unaltered, even after four or five pro-

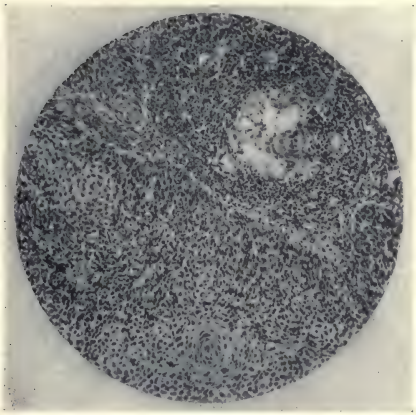

Fig. 4. M. M., June 6, 1916. Squamous-cell carcinoma before treatment.

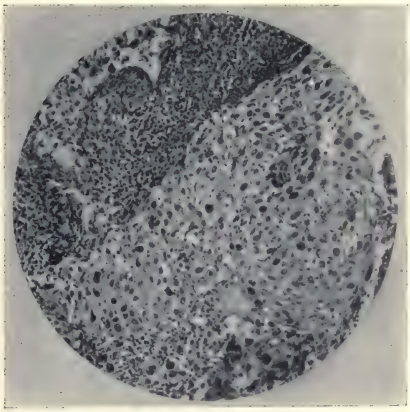

Fig. 5. M. M., June 14, 1916. Same eight days after 1000 mgm. hrs. of radiation. Note swelling of cells, enlargement and diffuse staining of nuclei.

longed exposures. This, of course, does not preclude the possibility that large quantities of radium, 500 to 1000 mgm., may perhaps exert a far deeper action. The majority of those who employ radium in pelvic disease, however, appear to agree that from 50 to 100 mgm. is the optimum amount to use.

The uterus removed from case 4, after eight radiations had been given, was cut in interrupted serial sections. In only two minute areas

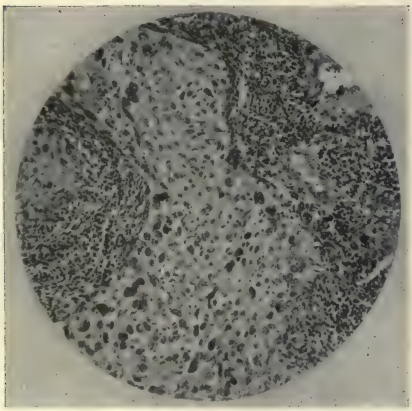

Fig. 6. M. M., June 23, 1916. Same seventeen days after beginning of treatment, 900 additional mgm. hrs. having been given. Note vacuolation of cells and increase in number of poorly staining nuclei.

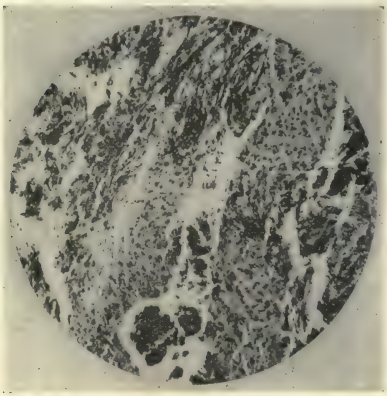

Fig. 7. M. M., July 3, 1916. Same twenty-seven days after beginning of of treatment, 4200 mgm hrs. of radiation. Note purulent exudate containing an occasional degenerating cancer cell.

were spots suggestive of degenerating carcinoma cells found. Figure 8 shows the carcinoma before treatment, and figure 9 the suggestive areas; this section was at a level well above the fornix at a distance of at least 3 or 4 cm. from the tip of the cervix

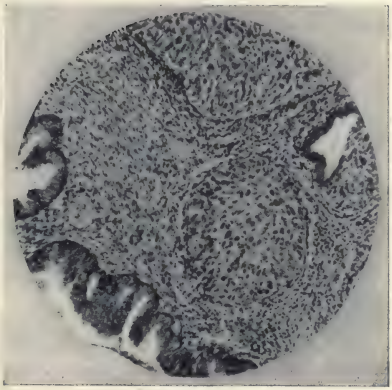

Fig. 8. P. G., February 11, 1916. Squamous-cell carcinoma in close proximity to cervical glands, before treatment.

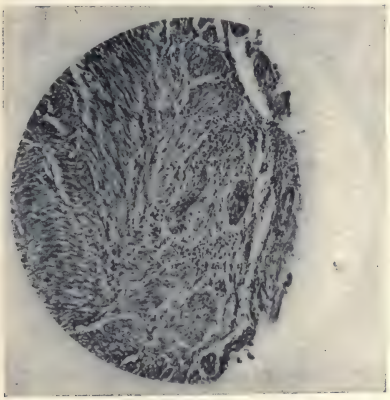

Fig. 9. P. G., April 3, 1916. Section from uterus removed per abdomen, seven weeks after beginning of treatment (five radiations aggregating 4600 mgm. hrs.). The entire uterus was cut and examined. The sole suspicious spots found are the two areas shown in the photomicrograph.

In view of the fact that the direct action upon cancer cells of the 120 mgm. of radium, as applied by the writer, does not manifest itself—when judged by histological criteria—beyond a distance of 1 to 1.5 cm., and yet at least temporary curative effects are observed over far wider areas *in the region of the cervix*, the writer is led to conclude that some other local factor must come into play. This local factor, in the case

Fig. 10. F. W., Sagittal section of the cervix removed nine days after the first radiation. Microscopically the cells appear unchanged and macroscopically the cervix looks infected and sloughy.

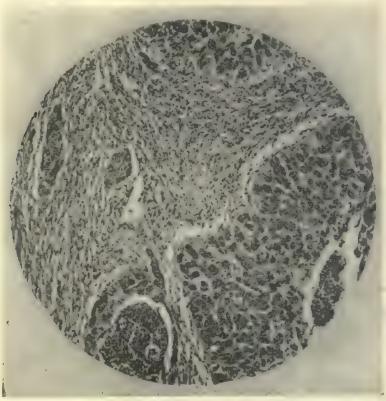

Fig. 11. F. W., May 1, 1916. Section from cervix of uterus removed per abdomen nine days after beginning of radiation (two radiations aggregating 2900 mgm. hrs.). The cancer cells (1 cm. from the surface) as yet show no changes, though their power of multiplication may be inhibited or destroyed. Higher power of fig. 10.

of cervical carcinoma, is probably supplied by the large quantity of connective tissue (parametria) which radiates from the cervix in all directions. Under the influence of the rays the connective tissue contracts, hardens, and perhaps proliferates. As a result, the lymphatics and smaller blood vessels are permanently blocked, and the dense scar pro-

duces a condition of "starvation" of the growth, a condition which has, at times, been obtained by surgical means (ligation of the internal iliac arteries). Further study is necessary and additional proof must be adduced before this suggestion can be accepted as more than a working hypothesis.

Histologically, carcinoma cells may appear normal and active, while biologically their growth and mitotic activity may either be inhibited or dead. This is especially true if the carcinomatous tissue is removed within eight to ten days after radiation. Figure 10 shows a sagittal section of the uterus removed in case 5, ten days after the first radiation had been given. The cells, when viewed with a high power (fig. 11) appear to be unchanged. Yet, though the vagina was cut across very close to the growth, no tendency to local recurrence was observed in the four weeks elapsing between operation and resumption of treatment.

Many further observations of interest and value can doubtless be made by close and persistent scrutiny of local excisions obtained during the course of treatment and of operative specimens obtained after preliminary radiation.

The following conclusions are warranted in the present state of our knowledge:

1. Radium is our best palliative measure in inoperable carcinoma of the cervix.

2. Far advanced cases may be treated with radium.

3. Radium not only rapidly relieves the pain, hemorrhage, and discharge, but indirectly also improves the general health and condition.

4. The minimum quantity of radium substance needed is 50 mgm.

5. "Border line" cases or operable cases should be submitted to operation after a short preliminary course of radiation. Good primary results may then be expected from simple total hysterectomy.

6. Operated cases should be subjected to postoperative, prophylactic radiation, beginning not later than four weeks after operation.

7. The technique of radium treatment of cervical cancer is simple and easy to learn.

In conclusion, a word of warning must be given against the building of undue hopes upon this recent addition to our weapons in the fight against cancer. The above report of early results obtained agrees in the main with the favorable results reported by many others, and shows that radium is a wonderful *palliative*. Whether the *final results* will prove that radium can give a permanent cure of cancer is a mooted question. Judging from the limited penetrating power of the rays and the variation of resistance of different cancers, it seems probable that numerous disappointments will occur, and that in many cases positive harm will be done by enthusiasts who refuse to submit operable cancers to surgical operation

HISTORIES

Case 1. A. E., sixty years old. Eight treatments beginning December 3, 1915, ending June 27, 1916, total 9242 mgmhrs. Ankylosed right hip, severe cardiac. Three children. Menopause ten years ago For two years foul discharge, four weeks bleeding. Cervix composed of a friable, hard lobulated mass involving fornices and right parametrium. Microscopically squamous-cell carcinoma.

After being well for eight months, with exception of rectal tenesmus, is now losing weight and strength. No local recurrence or metastases found.

Case 2. D. Z., forty-eight years old. Repeated cauterizations, tying off of vaginal branches of uterine arteries. Last cauterization December 28, 1915. Crater from cauterizations, left parametrium infiltrated. Microscopically carcinoma. Five radiations, beginning January 4, 1916, ending March 31, total 5029 mgmhrs. At present feels and looks well. No general or local signs of recurrence.

Case 3. D. E., thirty-three years old. Radical operation for carcinoma of cervix ten months before admission; reoperated for vaginal recurrence July, 1915. Since then repeated vaginal hemorrhages. Again operated December, 1915. On admission February 3, 1916, vault occupied by infiltration extending into both parametria and on right side extending almost to mucosa of rectum. No material for microscopic examination. Six radiations beginning February 3, 1916, ending July 18, total 6286 mgmhrs. At present feels and looks well, no infiltration or signs of recurrence or metastases.

Case 4. P. G., forty-two years old. Two abortions, operated at Mt. Sinai Hospital in 1912 for intraligamentous cyst, vaginal bleeding daily for three months. A red granular mass has substituted the posterior lip of the cervix infiltrating the right and posterior vaginal fornix (possibly still operable). Microscopically squamous-cell carcinoma. Five radiations beginning February 11, 1916, ending March 21, total 4629 mgmhrs. Total abdominal hysterectomy April 3, without excision of parametria. Uterus embedded in glistening white stony hard scar tissue. Uneventful convalescence except ureterovaginal fistula for four weeks. At present looks and feels well. No signs of local or general recurrence.

Uterus showed only two small microscopic areas suggestive of cancer cells.

Case 5. F. W., fifty years old; menopause three years ago, bleeds daily for eight months, has lost weight and strength. Entire cervix, especially posterior lip, is hypertrophic, uneven, bleeding freely to touch, parametria free (operable?). Microscopically squamous-cell carcinoma. Two radiations beginning April 22, 1916, ending April 28, total 2984 mgmhrs. May 1, complete hysterectomy without excision of parametria. Microscopically the carcinoma cells are unchanged (figs. 10 and 11). Three additional radiations given, beginning May 29, ending July 29, total of 8132 mgmhrs. in five sessions. At present feels and looks well. No signs of local or general recurrence.

Case 6. M. M., sixty-two years old. Eleven children, menopause fifteen years ago, foul discharge for two years, bleeding ten weeks. Obese, emphysematous, potatrix. The cervix consists of a bulging mass, extending into left fornix and infiltrating the upper part of the recto and vesicovaginal septa. Microscopically squamous-cell carcinoma. Six radiations, total 8077 mgmhrs., beginning June 6, 1916, ending July 27. Has had severe attack of articular rheumatism. No local signs of recurrence. At present is losing weight and strength, liver enlarged and nodular.

Case 7. W. M., fifty-two years old. No pregnancies, menstruation regular until one year ago, since then meno- and metrorrhagia; lost twenty pounds in six months. Cauterized repeatedly for inoperable squamous-cell carcinoma before admission, but without relief. Crater

infiltration of all vaginal walls to within 3 cm. of introitus, especially in vault, marked in vesicovaginal septum. Four radiations beginning August 16, 1916, ending October 5, total 10,905 mgmhrs. At present looks and feels well. Upper vaginal vault hard, uterus retroflexed, not freely movable. By rectum vaginal vault feels free, the right parametrium is doubtful.

Case 8. L. Z., fifty-seven years old. Ten pregnancies, menopause thirteen years ago, has been spotting eight months. Upper third of vagina infiltrated, vault rigid, cervix crater like, infiltration of vesico- and rectovaginal septum. *X*-ray shows pathological fracture of neck of right shoulder. Microscopically squamous-cell carcinoma. Four radiations beginning September 11, 1916, and to be continued, total to date 6070 mgmhrs. Crater (November 11) smaller, no bleeding, much improved in health. *X*-ray shows progress of arm lesion.

Case 9. C. Prophylactic radiation after Wertheim hysterectomy (May, 1915) 1660 mgmhrs. At present well.

Case 10. C. G. Prophylactic radiation after Wertheim hysterectomy June, 1915, 1880 mgmhrs.

REVIEWS AND ABSTRACTS.

Gaston Torrence, M. D., W. C. Gewin., M. D., and Walter A. Weed, M. D. (Birmingham, Ala.). The Use of Radium in Malignant and Non-Malignant Conditions with Report of Cases. The Charlotte Medical Journal, Vol. LXXIV, No. 5, Nov., 1916, pp. 205-11. Read before the Chattahoochie Valley Medical and Surgical Association, July, 1916.

RESUME OF CASES. EPITHELIOMATA.

"Of sixteen cases treated, six are apparently cured, four improved, two, in which it is too early to note results, one improved, but has not returned for further treatment, and one died."

"The treatment of epitheliomata by means of radium has, on the whole, been very gratifying. Cases, in which only the cutaneous surface is involved, have responded promptly."

"Epitheliomata of the cutaneous surface, if flat and superficial, and not accompanied by ulceration are given from 20 to 100 Mg. hours, using a flat half strength applicator, with no screening except one thickness of pure rubber dam. If the cosmetic effect is to be considered screening up to 1 mm. of silver may be used with a corresponding increase in the length of exposure."

"Where there is much infiltration it is necessary to use the tubes of radium in order to increase the intensity and depth of exposure. The deeper the infiltration, the more screening necessary with a prolonged exposure. Often as much as 100 mg. is used screened with 1 mm. of silver, and applied for 24 hours. This is given in four to six hours' exposure extending over a period of four to six days."

"Epitheliomata of the mucous surface are much more obstinate than when only the skin is affected. Where the growth is near a mucocutaneous junction it is desirable to give radium treatment before it reaches the mucous surface, as a much more favorable prognosis may be given."

"Melanotic epitheliomata, as well as melonotic sarcoma, are apparently but little influenced by radium. We have had only one case of this type, which was operated upon by the Drs. Mayo of Rochester with a most unfavorable prognosis. At the time radium treatment was begun there were metastases in the chest. The progress of the disease was not checked, but the pain was greatly relieved by the radium applications."

"Six of the cases had been treated previously by the X-ray. Of these three are apparently cured, one very much improved, one, unimproved, and one, in which insufficient time has elapsed to note results."

"The cases that have shown no improvement were very unfavorable to begin with because of the advanced stage of the disease, or inaccessibility of the growth."

Carcinomata of the Breast.—"Of five cases treated radium was used in four of them immediately after operation as a prophylactic measure against recurrence. The other case was one of recurrence two years after operation. She was in a hopeless condition when first seen, and was advised that the treatment would only be palliative."

"All operable cases of cancer of the breast should be operated upon before using radium. The progress of inoperable cases is much retarded, and the pain lessened."

Carcinoma of the Uterus.—"Of four cases treated, two are apparently cured, one improved, and one the results not known, as she did not return for further treatment."

"The treatment of carcinoma of the uterus with radium has been very satisfactory. Of the two cases that are apparently cured one had a fungating growth of the cervix, which completely filled the upper part of the vagina. The case was first treated by placing 200 mg. of radium element, well screened, in the vagina in close proximity to the growth. The growth was completely gone in about six weeks. 100 mg. of radium was then placed in the cavity of the uterus and left for five hours on three successive days, making a total exposure of 1500 mg. hours. There are no further symptoms and the patient is gaining in weight."

"The other case was one of the "excavating type" of carcinoma of the cervix involving the body of the uterus. The tumor had been cauterized by Dr. Baker of Charleston, S. C., who pronounced it inoperable and advised her to seek radium treatment."

"At the time she came for treatment the cervix was entirely gone; the uterus was completely fixed, there was considerable hemorrhage, and a very profuse discharge. Since treatment there is no hemorrhage, or discharge, and she is in excellent health."

"The case that is designated as "improved" was one, in which the uterus, the cervix, and broad ligaments all were involved, and was in a very advanced stage when first seen. No hope was entertained from the beginning so far as a cure was concerned, but it has been surprising how much improvement has taken place. The subsidence of the pain and offensive discharge has added very materially to her comfort. Also, no doubt her life will be considerably prolonged."

"The other patient was almost in a moribund condition when first seen, and was advised that treatment at best would be only palliative. We have not heard from her since she left the hospital."

Carcinoma of the Rectum.—"Of two cases treated one was too

far advanced to expect permanent improvement. The uterus and adjacent tissues were a large cancerous mass. The rectum, also, was extensively involved. A colostomy was done in March, 1916, by Dr. C. C. Cody of Houston, Texas, which was performing its function admirably. Radium treatment was given in June, 1916. We have not heard from her since treatment."

"The other case is still under treatment. Since beginning the radium applications the pain has almost completely subsided, the bowel derangement is very much lessened, and, on the whole, the patient is much more comfortable."

"As this patient is an elderly lady, and is already cachectic, what we hope to do is to control the pain, keep the bowel patent, and thus avoid the disagreeableness of a colostomy."

Carcinoma of the Bladder.—"The only case of carcinoma of the bladder treated was a secondary condition following cancer of the uterus, which was referred by Dr. O. P. Board of Birmingham. This patient had a total hysterectomy at St. Thomas' Hospital, Nashville, for carcinoma of the uterus in November, 1914. She remained apparently well until February, 1916, when she noticed blood and shreds in the urine. The bleeding was profuse at times. When seen April, 1916, cystoscopic examination revealed a rather extensive involvement of the bladder about the trigone. Radium treatment was given by introducing tubes of radium into the bladder. She returned for treatment in June following; at this time the symptoms had entirely disappeared, and cystoscopic examination showed a very decided improvement of the local condition."

Paget's Disease of the Breast—"In one case treated the superficial lesion was entirely cured by the first treatment. The nodule in the breast, which was about the size of a hen-egg, was materially lessened; and a letter from her states that it is still decreasing in size since the second treatment."

Sarcoma of Breast—"The relief in one case treated was only palliative, as there were metastases of the long bones, and mediastinum when she came for treatment."

Sarcoma of Parotid Gland.—" We have had two cases which were both in an advanced stage when first seen. One case had been operated upon for tumor of the breast (supposedly sarcoma) about two years ago. At the time treatment was given there were two growths about the size of large marbles near the original breast incision, one nodule about the same size on top of the head, and a large tumor of the parotid gland; and, also, probable involvement of the mediastinum. The radium made her much more comfortable, but did not check the progress of the disease."

"The other case has been under observation but a short time. No definite results have been noticed."

"Sarcoma of the Intestine.—"Of two cases treated one has been under treatment but a short time. She was operated upon in May, 1915, by Deaver of Philadelphia, for a retro-peritoneal tumor which proved to be fibro-sarcoma. She has a rather large recurrent intra-abdominal mass. Since beginning radium treatment the pain has subsided and, on the whole, the patient is feeling much better. Insufficient time has elapsed to expect a marked retrogression of tumor."

"The other case was referred by Dr. W. P. McAdory of Birming-

ham, who, on February 12, 1916, removed a tumor of the ilium and mesentery. About three feet of intestine was excised. Pathological examination showed the tumor to be sarcoma. About July 1st he was referred by Dr. McAdory for radium treatment. At that time there was a palpable tumor apparently as large as a man's fist. Also he had diarrhoea, and a very foul odor of breath. At times he suffered considerable pain. Treatment was given from July 7th to 13th, inclusive."

"He returned for second treatment on August 10th. Patient's condition was much improved; the foul odor of breath had entirely disappeared, bowels were normal, suffered very little pain, and the growth was appreciably smaller."

Goitre.—"Two goitres have been treated; one exophthalmic, and one simple."

"The exophthalmic goitre improved rapidly. The tachycardia gradually subsided, the gland reduced in size, and the nervousness disappeared."

"The pain caused by the pressure of the simple goitre soon subsided, even though there has been no noticeable decrease in the size of the gland."

Hodgkin's Disease.—"Only one case has been treated which was referred by Dr. Gaston Greil of Montgomery. Dr. Greil operated on her in July, 1914, removing glands of right side of neck."

"Dr. Greil referred her for radium treatment on June 27, 1916. At that time she was thin and emaciated. There was enlargement of the glands near the angle of the right lower maxilla, also of left supraclavicular glands."

"After giving radium treatment she seemed to improve for a few weeks. Since then a letter states that she had lapsed back to about the same condition as she was in when treatment was given."

Fibroids of Uterus.—"Three cases of fibroids of the uterus have been treated, all of which are clinically cured."

"The treatment of fibroids, when not too large and accompanied by menorrhagia or metrorhagia is highly satisfactory."

"The cases treated have responded promptly. The discharge and hemorrhage has entirely stopped, and the fibroids have decreased in size."

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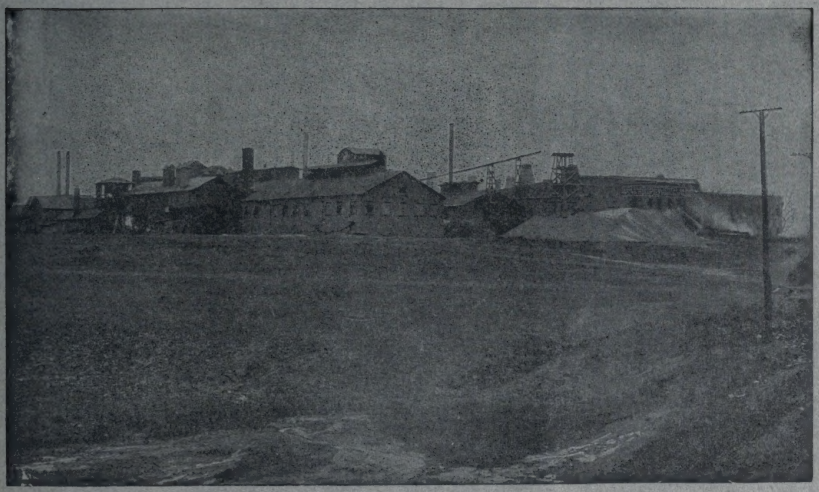

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